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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	3	JAN 16	CA/CAPplus Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	6	JAN 22	CA/CAPplus updated with revised CAS roles
NEWS	7	JAN 22	CA/CAPplus enhanced with patent applications from India
NEWS	8	JAN 29	PHAR reloaded with new search and display fields
NEWS	9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	13	FEB 26	MEDLINE reloaded with enhancements
NEWS	14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	19	MAR 16	CASREACT coverage extended
NEWS	20	MAR 20	MARPAT now updated daily
NEWS	21	MAR 22	LWPI reloaded
NEWS	22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	26	APR 30	CA/CAPplus enhanced with 1870-1889 U.S. patent records
NEWS	27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	28	MAY 01	New CAS web site launched
NEWS	29	MAY 08	CA/CAPplus Indian patent publication number format defined
NEWS	30	MAY 11	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS EXPRESS			NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 08:26:26 ON 15 MAY 2007

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 08:26:36 ON 15 MAY 2007

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STRUCTURE FILE UPDATES: 14 MAY 2007 HIGHEST RN 934733-40-1

DICTIONARY FILE UPDATES: 14 MAY 2007 HIGHEST RN 934733-40-1

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

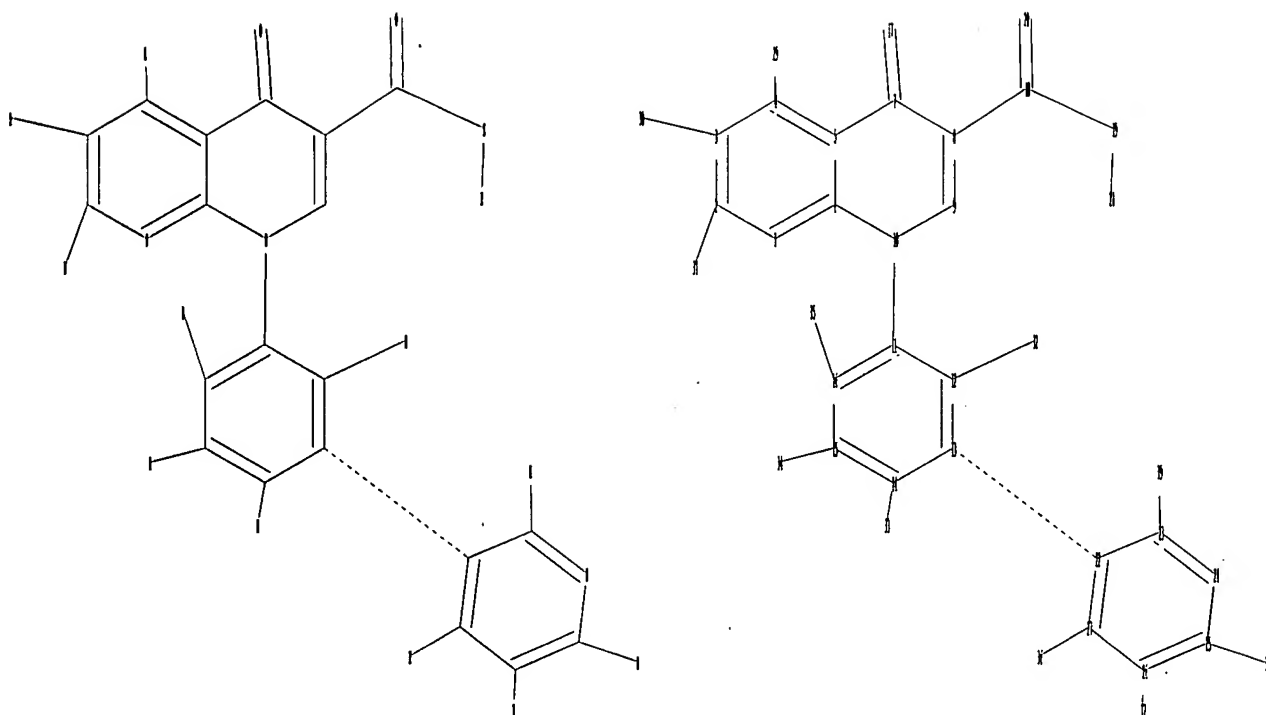
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<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10530465.str



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chain nodes :
17 18 19 20 21 29 30 31 32 33 34 35 36 37 38 39
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 22 23 24 25 26 27
chain bonds :
2-31 3-30 4-29 7-17 8-18 10-11 12-32 13-22 14-33 15-34 16-35 18-19
18-20 19-21 23-39 25-38 26-37 27-36
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 22-23 22-27 23-24 24-25 25-26 26-27
exact/norm bonds :
5-7 6-10 7-8 7-17 8-9 9-10 10-11 13-22 18-19 18-20
exact bonds :
2-31 3-30 4-29 8-18 12-32 14-33 15-34 16-35 19-21 23-39 25-38 26-37
27-36
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 22-23
22-27 23-24 24-25 25-26 26-27
isolated ring systems :
containing 1 : 11 : 22 :

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Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS
38:CLASS 39:CLASS

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L1        STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1        STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 08:27:06 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED -        2 TO ITERATE

100.0% PROCESSED        2 ITERATIONS

1 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:    ONLINE    \*\*COMPLETE\*\*

BATCH    \*\*COMPLETE\*\*

PROJECTED ITERATIONS:        2 TO        124

PROJECTED ANSWERS:        1 TO        80

L2        1 SEA SSS SAM L1

=> s l1 full

FULL SEARCH INITIATED 08:27:11 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED -        66 TO ITERATE

100.0% PROCESSED        66 ITERATIONS

8 ANSWERS

SEARCH TIME: 00.00.01

L3        8 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

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172.31

FILE 'CAPLUS' ENTERED AT 08:27:15 ON 15 MAY 2007

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FILE COVERS 1907 - 15 May 2007 VOL 146 ISS 21

FILE LAST UPDATED: 14 May 2007 (20070514/ED)

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<http://www.cas.org/infopolicy.html>

=> s l3 full

L4        4 L3

=> d ibib abs hitstr tot

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:467891 CAPLUS  
DOCUMENT NUMBER: 141:38597  
TITLE: Preparation of aryl substituted 1,8-naphthyridin-4(1H)-  
ones as inhibitors of phosphodiesterase-4  
INVENTOR(S): Albaneze-Walker, Jennifer; Murry, Jerry Anthony;  
Soheili, Arash; Springfield, Shawn A.  
PATENT ASSIGNEE(S): Merck & Co., Inc., USA  
SOURCE: PCT Int. Appl., 142 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004048377	A2	20040610	WO 2003-US36806	20031118
WO 2004048377	A3	20040902		
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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2506656	A1	20040610	CA 2003-2506656	20031118
AU 2003291050	A1	20040618	AU 2003-291050	20031118
EP 1565466	A2	20050824	EP 2003-783636	20031118
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003016464	A	20051011	BR 2003-16464	20031118
CN 1738818	A	20060222	CN 2003-80108946	20031118
JP 2006513271	T	20060420	JP 2005-510366	20031118
US 2006019981	A1	20060126	US 2005-530465	20050405
NO 2005003047	A	20050810	NO 2005-3047	20050621
PRIORITY APPLN. INFO.:			US 2002-428315P	P 20021122
			US 2003-472655P	P 20030522
			WO 2003-US36806	W 20031118
OTHER SOURCE(S):	MARPAT 141:38597			
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB In one aspect, the present invention is directed to a one pot method of preparing intermediates I [OR1 = a suitable leaving group; R3 = (un)substituted alkyl, aryl, heteroaryl], which are useful in making inhibitors of phosphodiesterase-4. The present invention is also directed to a method of preparing phosphodiesterase inhibitors (no biol. data given) comprising the compds. II and III which comprises reacting IV [OR1 as above] with a 3-bromopyridine-N-oxide.HCl or 3-bromopyridine in the presence of a palladium catalyst and a phosphine ligand in amine base followed by reaction of the resulting V or VI with cyclopropylamine, optionally in the presence of catalyst. Thus, reacting IV [R1 = Et] with a 3-bromopyridine-N-oxide.HCl in the presence of [(allyl)PdCl]2, P(tert-Bu)3, tert-amylamine in DMAc followed by reacting V [R1 = Et] with

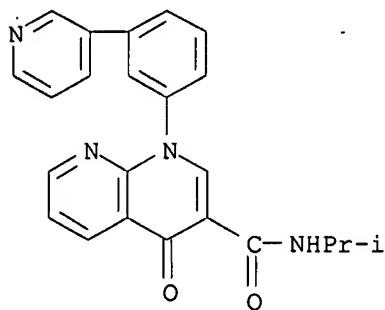
cyclopropylamine afforded II. Preparation of 77 aryl substituted 1,8-naphthyridin-4(1H)-ones and their intermediates is also described.

IT 477251-87-9P 477251-95-9P 694489-52-6P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4)

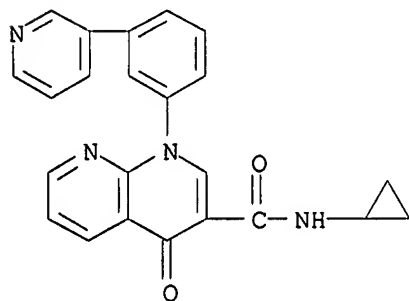
RN 477251-87-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



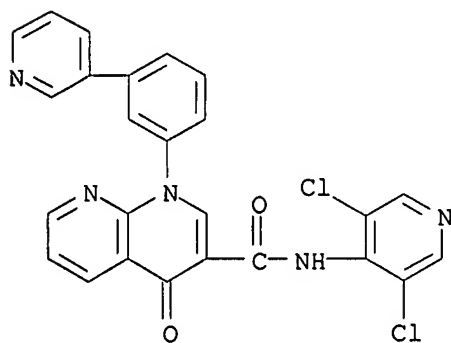
RN 477251-95-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 694489-52-6 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



IT 477252-44-1P 477252-50-9P 694489-58-2P

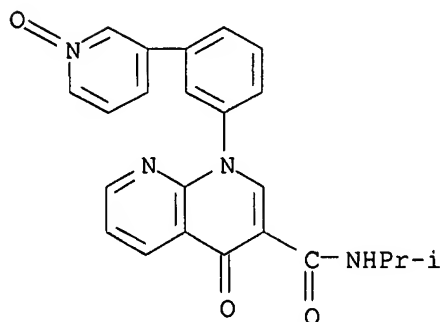
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
(Uses)

(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors  
of phosphodiesterase-4)

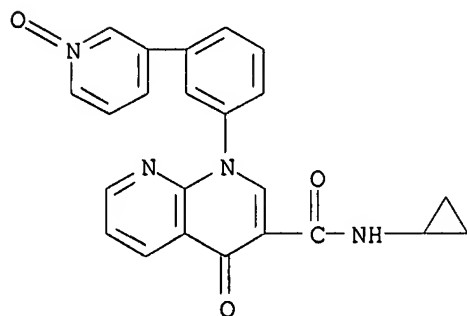
RN 477252-44-1 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-1-[3-(1-  
oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



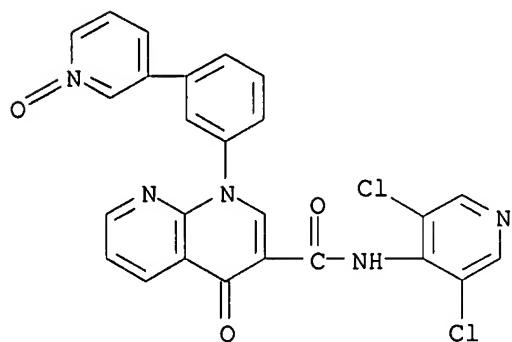
RN 477252-50-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-  
pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 694489-58-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-  
1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:467741 CAPLUS

DOCUMENT NUMBER: 141:38595

TITLE: Preparation of substituted naphthyridine

phosphodiesterase-4 inhibitors as enhancers of cognition

INVENTOR(S):

Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Girard, Yves; MacDonald, Dwight; Friesen, Richard; Ducharme, Yves; Cote, Bernard; Blouin, Marc; Martins, Evelyn; Guay, Daniel; Girard, Mario; Frenette, Richard; Laliberte, Sebastien; Robichaud, Annette; Mastracchio, Anthony; Perrier, Helene

PATENT ASSIGNEE(S):

Merck Frosst Canada & Co., Can.; Hamel, Pierre

SOURCE:

PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

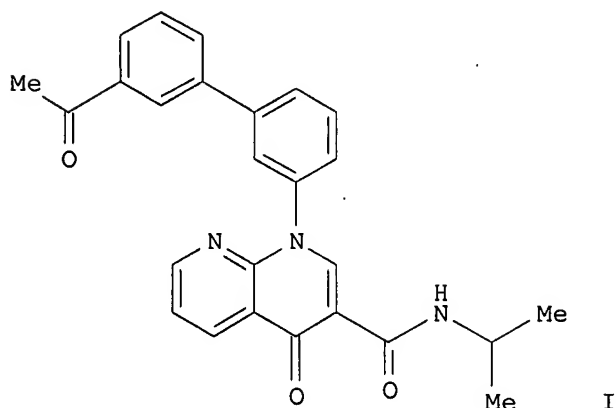
FAMILY ACC. NUM. COUNT:

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PATENT INFORMATION:

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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
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EP 1592419	A1	20051109	EP 2003-776698	20031119
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2006040981	A1	20060223	US 2005-536250	20050520
PRIORITY APPLN. INFO.:			US 2002-428541P	P 20021122
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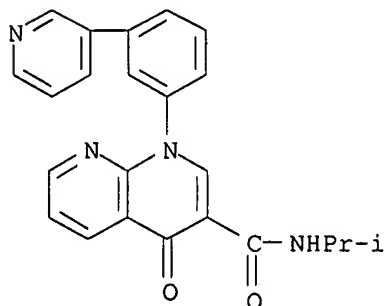


AB Substituted naphthyridines are prepared as PDE-4 inhibitors. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate (preparation given) is treated with NaH in THF to give Et 1-(3-bromophenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxylate. This intermediate is saponified, coupled to i-PrNH<sub>2</sub> (THF, Et<sub>3</sub>N, i-BuOCOC1) and coupled to 3-acetylphenylboronic acid (PhMe, EtOH, Na<sub>2</sub>CO<sub>3</sub>, trans-

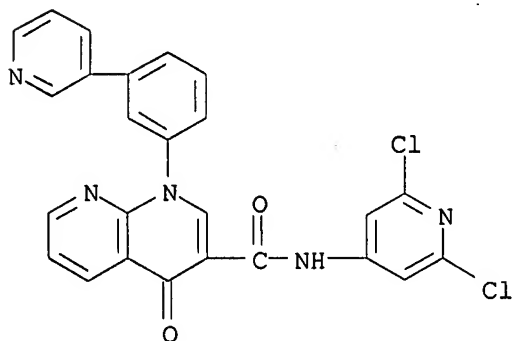


dibromobis(triphenylphosphine)palladium, reflux, 1 h) to give I. Example compds. have IC50 values of 0.1 to 90.0 nM for PDE4; these compds. are useful for enhancing memory, learning, retention, recall, awareness and judgement.

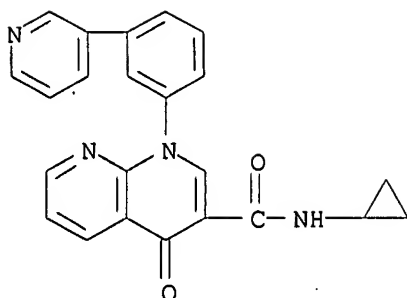
- IT 477251-87-9P, N-Isopropyl-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477251-91-5P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477251-95-9P, N-Cyclopropyl-1-[3-(pyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)  
 RN 477251-87-9 CAPLUS  
 CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



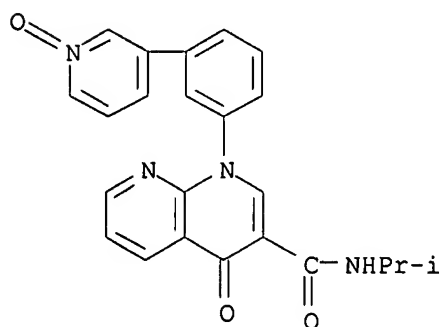
- RN 477251-91-5 CAPLUS  
 CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



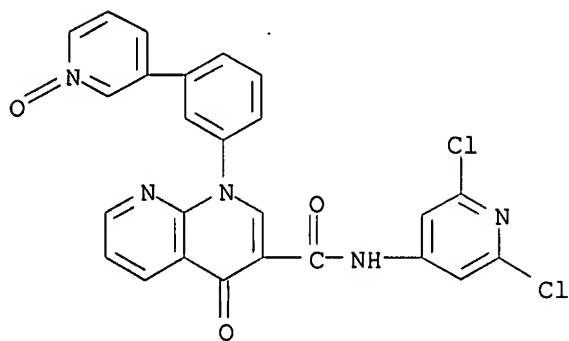
- RN 477251-95-9 CAPLUS  
 CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



IT 477252-44-1P, N-Isopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477252-45-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide 477252-50-9P, N-Cyclopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)  
 RN 477252-44-1 CAPLUS  
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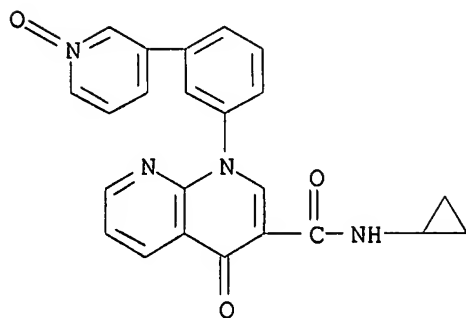


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RN 477252-50-9 CAPLUS  
 CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-

pyridinyl]phenyl]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:433770 CAPLUS

DOCUMENT NUMBER: 141:7041

TITLE: One-pot preparation of naphthyridine derivatives, useful as inhibitors of phosphodiesterase-4

INVENTOR(S): Albaneze-Walker, Jennifer; Ceglia, Scott; Murry, Jerry Anthony; Soheili, Arash

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 57 pp., which

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004102472	A1	20040527	US 2003-690118	20031021
US 6909002	B2	20050621		
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			US 2003-472598P	P 20030522
OTHER SOURCE(S):		CASREACT 141:7041; MARPAT 141:7041		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to one-pot preparation of naphthyridine derivs. of formula I [wherein: OR1 is a suitable leaving group; R2 is C1-8alkyl, (un)substituted (hetero)aryl], useful as inhibitors of phosphodiesterase-4 (no biol. data). For instance, naphthyridine derivative II was prepared via heterocyclization of Et 2-chloronicotinoylacetate, 3-bromoaniline, and acetic anhydride, hydrolysis of the obtained ester III (R3 = Br), amidation by isopropylamine, and subsequent phenylacetylation by 3-acetylphenylboronic acid (example 1, no yield data). Naphthyridine derivative IV was prepared using the prepared intermediate III [R3 = -B(OH)2]

(p. 49-53).

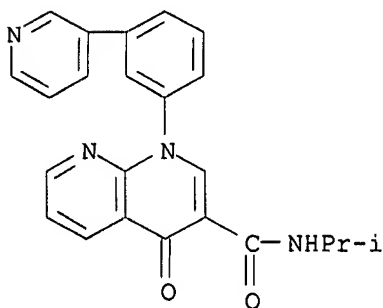
IT 477251-87-9P 477251-95-9P 694489-52-6P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(one-pot method of preparation of naphthyridine derivs. useful as inhibitors of phosphodiesterase-4)

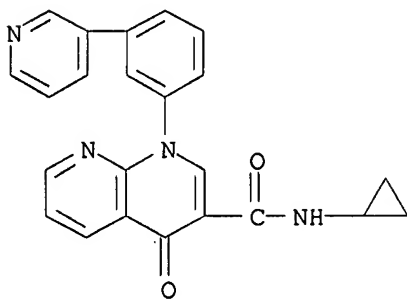
RN 477251-87-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



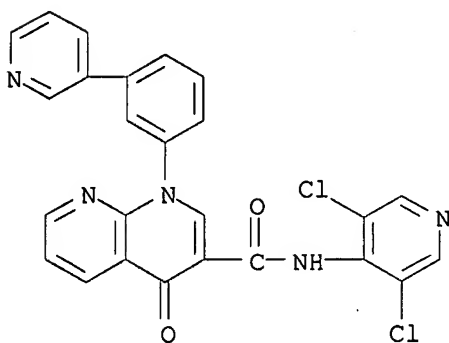
RN 477251-95-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 694489-52-6 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



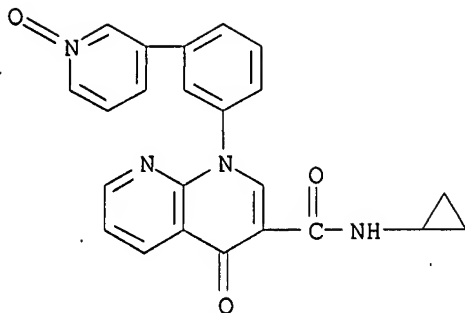
IT 477252-50-9P 694489-58-2P

RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(one-pot preparation of naphthyridine derivs., useful as inhibitors of phosphodiesterase-4)

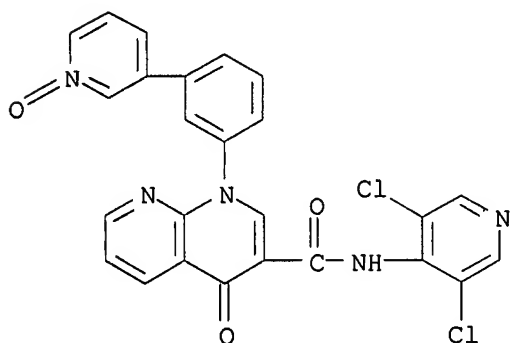
RN 477252-50-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 694489-58-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(3,5-dichloro-4-pyridinyl)-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:906219 CAPLUS

DOCUMENT NUMBER: 138:4594

TITLE: Preparation of 1-biaryl-[1,8]naphthyridin-4-one phosphodiesterase IV inhibitors for treatment of asthma and inflammation

INVENTOR(S): Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard; Girard, Yves; Li, Chun

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 166 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002094823	A1	20021128	WO 2002-CA746	20020522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2447765	A1	20021128	CA 2002-2447765	20020522

AU 2002257459	A1	20021203	AU 2002-257459	20020522
EP 1397359	A1	20040317	EP 2002-727127	20020522
EP 1397359	B1	20050831		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534773	T	20041118	JP 2002-591496	20020522
AT 303384	T	20050915	AT 2002-727127	20020522
ES 2247325	T3	20060301	ES 2002-2727127	20020522
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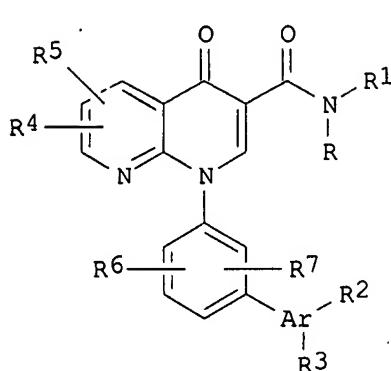
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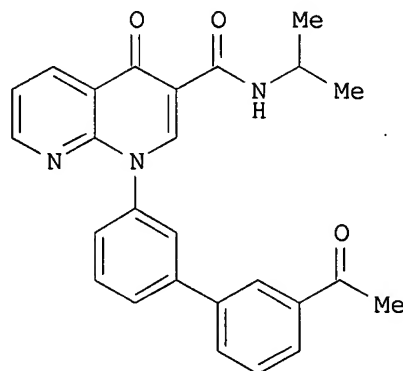
OTHER SOURCE(S):

MARPAT 138:4594

GI



I



II

AB Title compds. I [wherein Ar = Ph, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, or heteroaryl oxides; R = H or alkyl; R1 = H or (un)substituted (cyclo)alkyl, alkoxy, alkenyl, alkynyl, heteroaryl, or heterocyclyl; R2 = H, halo, (cyclo)alkyl, alkoxy, amino, acyl, alkoxy carbonyl, alkylsulfamoyl, alkylsulfonyl, or (un)substituted Ph, heteroaryl, or heterocyclyl, etc.; R3 = H, OH, NH2, halo, (un)substituted alkyl; R4-R7 = independently H, halo, NH2, or (un)substituted alkyl or alkoxy; or pharmaceutically acceptable salts thereof] were prepared as phosphodiesterase IV (PDE4) inhibitors for the treatment of asthma and inflammation. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate was cyclized using NaH in THF and the resulting ester saponified to give 1-(3-bromophenyl)-1,4-dihydro-[1,8]naphthyridine-4-one-3-carboxylic acid. Amidation with isopropylamine, followed by treatment with 3-acetylphenylboronic acid in the presence of trans-PdBr2(PPh3)2 and Na2CO3 in toluene and EtOH gave II. I demonstrated PDE4 inhibitory activity by suppression of TNF- $\alpha$  secretion in LPS stimulated human blood with IC50 values generally ranging from 0.005  $\mu$ M to 15.4  $\mu$ M. In a SPA based PDE activity assay, I inhibited the hydrolysis of cAMP to AMP by human recombinant phosphodiesterase IVa with IC50 values between 34.3 nM and 134.0 nM.

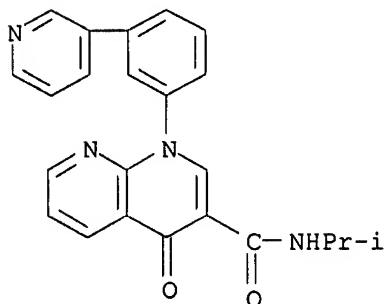
IT 477251-87-9P, N-Isopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-91-5P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477251-95-9P, N-Cyclopropyl-1-[3-(pyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(PDE4 inhibitor; preparation of biaryl naphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for treatment of asthma and inflammation)

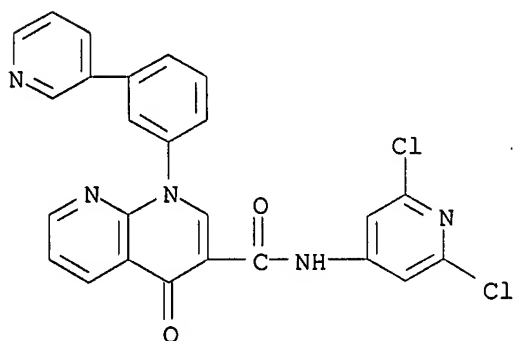
RN 477251-87-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME).



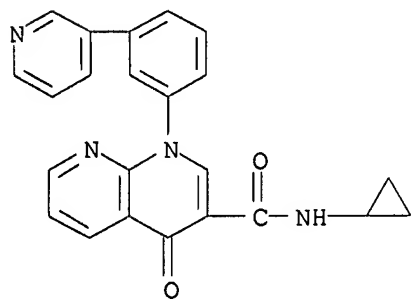
RN 477251-91-5 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



RN 477251-95-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-4-oxo-1-[3-(3-pyridinyl)phenyl]- (9CI) (CA INDEX NAME)



IT 477252-44-1P, N-Isopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-45-2P, N-(2,6-Dichloropyridin-4-yl)-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide 477252-50-9P, N-Cyclopropyl-1-[3-(1-oxidopyridin-3-yl)phenyl]-4-oxo-1,4-dihydro-[1,8]naphthyridine-3-carboxamide

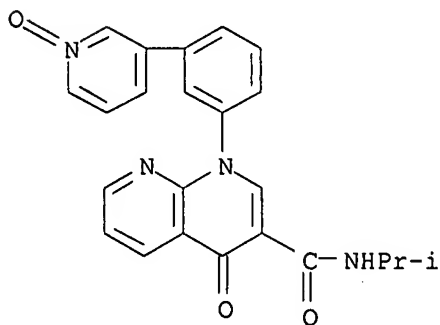
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4 inhibitor; preparation of biarylnaphthyridinone PDE4 inhibitors by cyclization and arylation of (arylamino)(nicotinoyl)acrylates for

treatment of asthma and inflammation)

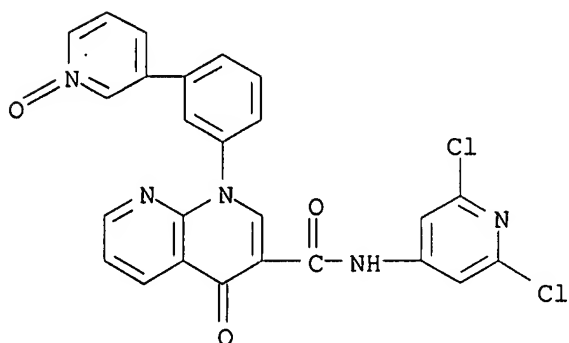
RN 477252-44-1 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



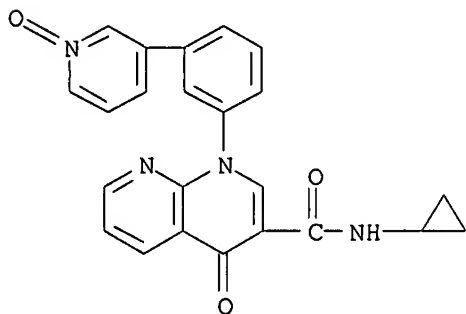
RN 477252-45-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-(2,6-dichloro-4-pyridinyl)-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



RN 477252-50-9 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-(1-oxido-3-pyridinyl)phenyl]-4-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:26:26 ON 15 MAY 2007)



FILE 'REGISTRY' ENTERED AT 08:26:36 ON 15 MAY 2007

L1           STRUCTURE UPLOADED  
L2           1 S L1  
L3           8 S L1 FULL

FILE 'CAPLUS' ENTERED AT 08:27:15 ON 15 MAY 2007

L4           4 S L3 FULL

=> log y

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

22.49

194.80

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-3.12

-3.12

STN INTERNATIONAL LOGOFF AT 08:29:13 ON 15 MAY 2007

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PASSWORD:

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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS	3	JAN 16	CA/CAPlus Company Name Thesaurus enhanced and reloaded
NEWS	4	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS	5	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data
NEWS	6	JAN 22	CA/CAPlus updated with revised CAS roles
NEWS	7	JAN 22	CA/CAPlus enhanced with patent applications from India
NEWS	8	JAN 29	PHAR reloaded with new search and display fields
NEWS	9	JAN 29	CAS Registry Number crossover limit increased to 300,000 in multiple databases
NEWS	10	FEB 15	PATDPASPC enhanced with Drug Approval numbers
NEWS	11	FEB 15	RUSSIAPAT enhanced with pre-1994 records
NEWS	12	FEB 23	KOREAPAT enhanced with IPC 8 features and functionality
NEWS	13	FEB 26	MEDLINE reloaded with enhancements
NEWS	14	FEB 26	EMBASE enhanced with Clinical Trial Number field
NEWS	15	FEB 26	TOXCENTER enhanced with reloaded MEDLINE
NEWS	16	FEB 26	IFICDB/IFIPAT/IFIUDB reloaded with enhancements
NEWS	17	FEB 26	CAS Registry Number crossover limit increased from 10,000 to 300,000 in multiple databases
NEWS	18	MAR 15	WPIDS/WPIX enhanced with new FRAGHITSTR display format
NEWS	19	MAR 16	CASREACT coverage extended
NEWS	20	MAR 20	MARPAT now updated daily
NEWS	21	MAR 22	LWPI reloaded
NEWS	22	MAR 30	RDISCLOSURE reloaded with enhancements
NEWS	23	APR 02	JICST-EPLUS removed from database clusters and STN
NEWS	24	APR 30	GENBANK reloaded and enhanced with Genome Project ID field
NEWS	25	APR 30	CHEMCATS enhanced with 1.2 million new records
NEWS	26	APR 30	CA/CAPlus enhanced with 1870-1889 U.S. patent records
NEWS	27	APR 30	INPADOC replaced by INPADOCDB on STN
NEWS	28	MAY 01	New CAS web site launched
NEWS	29	MAY 08	CA/CAPlus Indian patent publication number format defined
NEWS	30	MAY 11	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS EXPRESS			NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS			STN Operating Hours Plus Help Desk Availability
NEWS LOGIN			Welcome Banner and News Items
NEWS IPC8			For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 08:31:50 ON 15 MAY 2007

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 08:32:01 ON 15 MAY 2007

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FILE COVERS 1907 - 15 May 2007 VOL 146 ISS 21

FILE LAST UPDATED: 14 May 2007 (20070514/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.47	0.68

FILE 'CASREACT' ENTERED AT 08:32:07 ON 15 MAY 2007

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FILE CONTENT:1840 - 12 May 2007 VOL 146 ISS 21

New CAS Information Use Policies, enter HELP USAGETERMS for details.

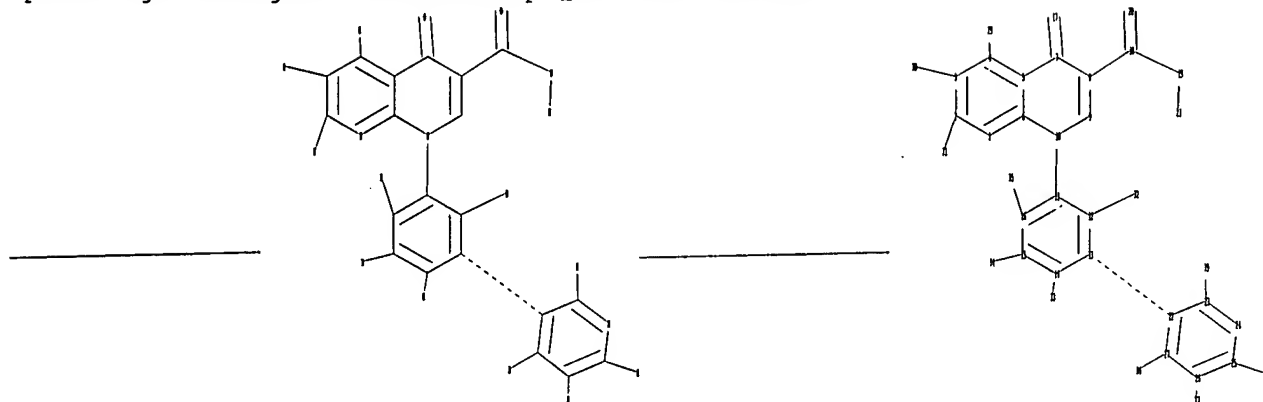
\*\*\*\*\*  
\* CASREACT now has more than 12 million reactions \*  
\* \*  
\*\*\*\*\*

Some CASREACT records are derived from the ZIC/VINITI database (1974-1999) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

Uploading C:\Program Files\Stnexp\Queries\10530465b.str



chain nodes :

17 18 19 20 21 29 30 31 32 33 34 35 36 37 38 39

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 22 23 24 25 26 27

chain bonds :

2-31 3-30 4-29 7-17 8-18 10-11 12-32 13-22 14-33 15-34 16-35 18-19  
18-20 19-21 23-39 25-38 26-37 27-36

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10 11-12 11-16 12-13 13-14  
14-15 15-16 22-23 22-27 23-24 24-25 25-26 26-27

exact/norm bonds :

5-7 6-10 7-8 7-17 8-9 9-10 10-11 13-22 18-19 18-20

exact bonds :

2-31 3-30 4-29 8-18 12-32 14-33 15-34 16-35 19-21 23-39 25-38 26-37  
27-36

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 11-12 11-16 12-13 13-14 14-15 15-16 22-23  
22-27 23-24 24-25 25-26 26-27

isolated ring systems :

containing 1 : 11 : 22 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:Atom 23:Atom 24:Atom 25:Atom 26:Atom 27:Atom 29:CLASS  
30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS 35:CLASS 36:CLASS 37:CLASS  
38:CLASS 39:CLASS

fragments assigned product role:

containing 1

L1 STRUCTURE UPLOADED

=> d 11

L1 HAS NO ANSWERS

L1 STR

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 08:32:44 FILE 'CASREACT'

SCREENING COMPLETE - 160 REACTIONS TO VERIFY FROM 3 DOCUMENTS

100.0% DONE 160 VERIFIED 22 HIT RXNS 1 DOCS  
SEARCH TIME: 00.00.01

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L2 ANSWER 1 OF 1 CASREACT COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 141:7041 CASREACT

TITLE: One-pot preparation of naphthyridine derivatives,  
useful as inhibitors of phosphodiesterase-4

INVENTOR(S): Albaneze-Walker, Jennifer; Ceglia, Scott; Murry, Jerry  
Anthony; Soheili, Arash

PATENT ASSIGNEE(S): Merck & Co., Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 57 pp., which  
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004102472	A1	20040527	US 2003-690118	20031021
US 6909002	B2	20050621		
PRIORITY APPLN. INFO.:			US 2002-428315P	20021122
			US 2003-472598P	20030522

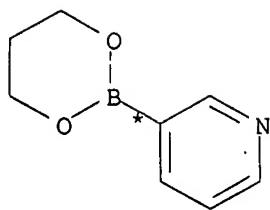
OTHER SOURCE(S): MARPAT 141:7041

GI

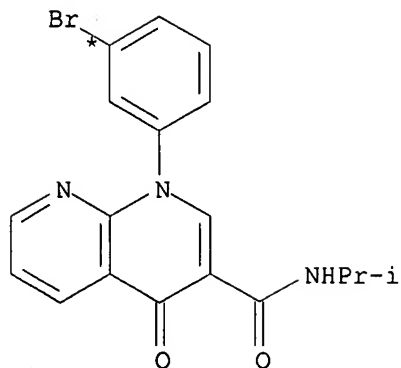
\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to one-pot preparation of naphthyridine derivs. of formula I [wherein: OR1 is a suitable leaving group; R2 is C1-8alkyl, (un)substituted (hetero)aryl], useful as inhibitors of phosphodiesterase-4 (no biol. data). For instance, naphthyridine derivative II was prepared via heterocyclization of Et 2-chloronicotinoylacetate, 3-bromoaniline, and acetic anhydride, hydrolysis of the obtained ester III (R3 = Br), amidation by isopropylamine, and subsequent phenylacetylation by 3-acetylphenylboronic acid (example 1, no yield data). Naphthyridine derivative IV was prepared using the prepared intermediate III [R3 = -B(OH)2] (p. 49-53).

RX(12) OF 305 ...AL + B ==> AM

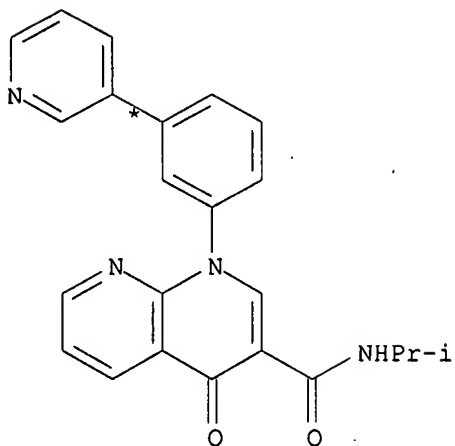


AL



B

(12) →



AM

RX(12) RCT AL 131534-65-1, B 477251-79-9  
 RGT D 497-19-8 Na<sub>2</sub>CO<sub>3</sub>  
 PRO AM 477251-87-9  
 CAT 72287-26-4 Palladium, [1,1'-bis(diphenylphosphino-  
 κP)ferrocene]dichloro-, (SP-4-2)-  
 SOL 7732-18-5 Water, 64-17-5 EtOH  
 CON 1 hour, reflux

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 08:31:50 ON 15 MAY 2007)

FILE 'CAPLUS' ENTERED AT 08:32:01 ON 15 MAY 2007

FILE 'CASREACT' ENTERED AT 08:32:07 ON 15 MAY 2007

L1 STRUCTURE UPLOADED  
 L2 1 S L1 FULL

=> log y  
 COST IN U.S. DOLLARS

SINCE FILE TOTAL  
 ENTRY SESSION

FULL ESTIMATED COST	118.92	119.60
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
CA SUBSCRIBER PRICE	ENTRY	SESSION
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STN INTERNATIONAL LOGOFF AT 08:33:19 ON 15 MAY 2007

=&gt; s 13

L4 7 L3

=&gt; d abs bib fhitr 1-7

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AB This invention relates to dry power aerosol formulations for use with a dry powder inhaler, the formulation comprising the PDE 4 inhibitor N-cyclopropyl-1-[3-(1-oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide. An investigation into the aerosol performance of the above drug with different grades of lactose at 4% drug loading demonstrated that sieved lactose was the most suitable carrier of the 3 choices. Granulated lactose produced the weakest drug aerosolization compared to milled and sieved lactose.

AN 2007:356793 CAPLUS

DN 146:323609

TI Aerosol powder formulation

IN Thibert, Roch; Meisner, Dale; Rossi, Joanna; Tanfara, Helen

PA Can.

SO U.S. Pat. Appl. Publ., 10pp.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2007071692	A1	20070329	US 2006-528107	20060927
	WO 2007036029	A1	20070405	WO 2006-CA1583	20060926
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
	RW:				
	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

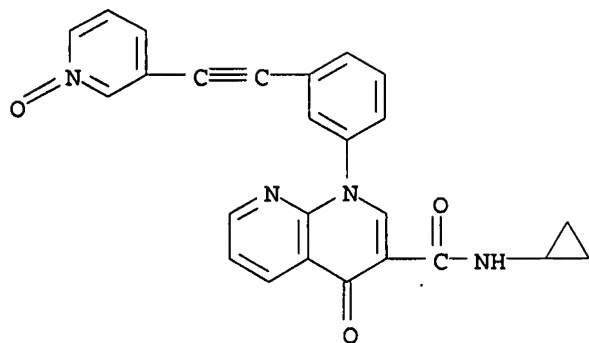
PRAI US 2005-721402P P 20050928

IT 500355-52-2, N-Cyclopropyl-1-[3-(1-oxido-3-pyridinylethynyl)phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (aerosol powder formulation)

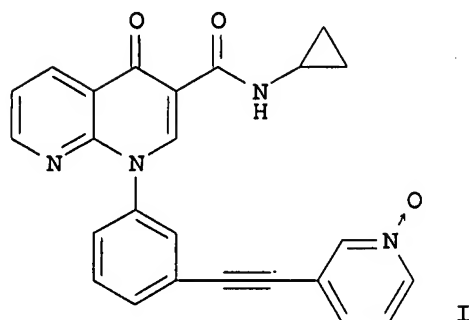
RN 500355-52-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)





L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
GI



AB The present invention is directed to alternative forms of the title phosphodiesterase 4 inhibitor (I). I was prepared from Et 4-oxo-1,4-dihydro-4-(3-ethynylphenyl)-1,8-naphthyridine-3-carboxylate and 3-bromopyridine N-oxide giving an ester which was then treated with cyclopropylamine. Polymorphic forms such as the hemihydrate, anhydrous form, dihydrate, and monohydrate were prepared

AN 2005:1200294 CAPLUS

DN 143:460135

TI Preparation of polymorphic forms of the phosphodiesterase-4 inhibitor N-cyclopropyl-1-{3-[(1-oxidopyridin-3-yl)ethynyl]phenyl}-4-oxo-1,4-dihydro-1,8-naphthyridine-3-carboxamide

IN Clas, Sophie-Dorothee; Naccache, Rafik; Yu, Hongshi; Murry, Jerry; Variankaval, Narayan

PA Merck Frosst Canada Ltd., Can.; Merck & Co., Inc.

SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2

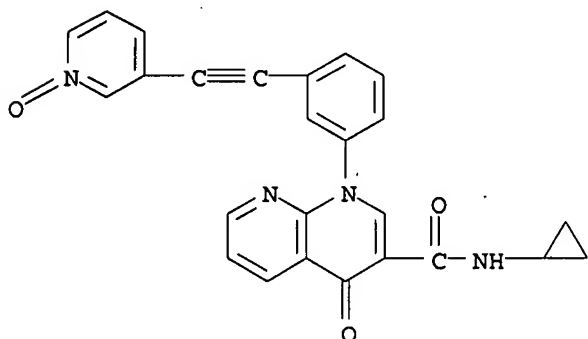
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005105084	A1	20051110	WO 2005-US13853	20050422
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,				

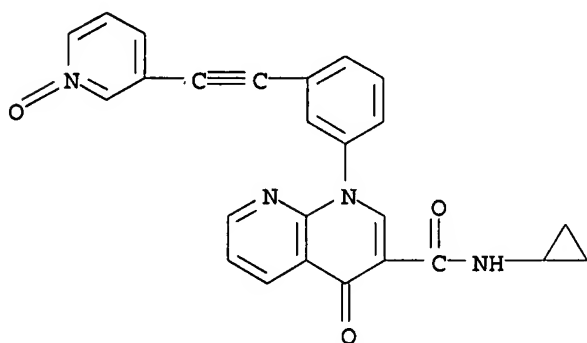
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,  
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,  
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,  
ZM, ZW  
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
MR, NE, SN, TD, TG  
EP 1742628 A1 20070117 EP 2005-738340 20050422  
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR  
PRAI US 2004-565446P P 20040426  
WO 2005-US13853 W 20050422  
IT 500355-52-2P  
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);  
BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of polymorphic forms of phosphodiesterase-4 inhibitor  
N-cyclopropyl-1-{3-[(1-oxidopyridin-3-yl)ethynyl]phenyl}-4-oxo-1,4-  
dihydro-1,8-naphthyridine-3-carboxamide)  
RN 500355-52-2 CAPLUS  
CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-  
oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
AB The invention discloses the treatment or prevention of diseases involving  
deposition of  $\beta$ -amyloid in the brain, e.g. Alzheimer's disease, via  
the combined administration of a growth hormone secretagogue and a PDE4  
inhibitor.  
AN 2004:857402 CAPLUS  
DN 141:325764  
TI Growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for  
the treatment of Alzheimer's disease  
IN Castro Pineiro, Jose Luis  
PA Merck Sharp & Dohme Limited, UK  
SO PCT Int. Appl., 20 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004087157	A2	20041014	WO 2004-GB1435	20040401
	WO 2004087157	A3	20041118		
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	AU 2004226698	A1	20041014	AU 2004-226698	20040401
	CA 2521046	A1	20041014	CA 2004-2521046	20040401
	CN 1764457	A	20060426	CN 2004-80008035	20040401
	EP 1660086	A2	20060531	EP 2004-725099	20040401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
	JP 2006522084	T	20060928	JP 2006-506077	20040401
	US 2006183764	A1	20060817	US 2005-552367	20051003
PRAI	GB 2003-7863	A	20030404		
	WO 2004-GB1435	A	20040401		
IT	500355-52-2				
	RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (growth hormone secretagogue-phosphodiesterase 4 inhibitor combination for treatment of Alzheimer's disease)				
RN	500355-52-2 CAPLUS				
CN	1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)				



L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB In one aspect, the present invention is directed to a one pot method of

preparing intermediates I [OR1 = a suitable leaving group; R3 = (un)substituted alkyl, aryl, heteroaryl], which are useful in making inhibitors of phosphodiesterase-4. The present invention is also directed to a method of preparing phosphodiesterase inhibitors (no biol. data given) comprising the compds. II and III which comprises reacting IV [OR1 as above] with a 3-bromopyridine-N-oxide.HCl or 3-bromopyridine in the presence of a palladium catalyst and a phosphine ligand in amine base followed by reaction of the resulting V or VI with cyclopropylamine, optionally in the presence of catalyst. Thus, reacting IV [R1 = Et] with a 3-bromopyridine-N-oxide.HCl in the presence of [(allyl)PdCl]<sub>2</sub>, P(tert-Bu)<sub>3</sub>, tert-amylamine in DMAc followed by reacting V [R1 = Et] with cyclopropylamine afforded II. Preparation of 77 aryl substituted 1,8-naphthyridin-4(1H)-ones and their intermediates is also described.

AN 2004:467891 CAPLUS

DN 141:38597

TI Preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4

IN Albaneze-Walker, Jennifer; Murry, Jerry Anthony; Soheili, Arash; Springfield, Shawn A.

PA Merck &amp; Co., Inc., USA

SO PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

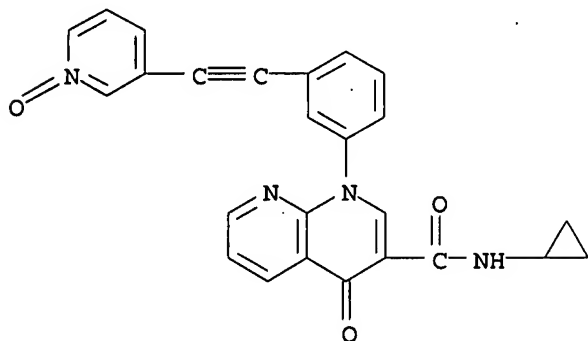
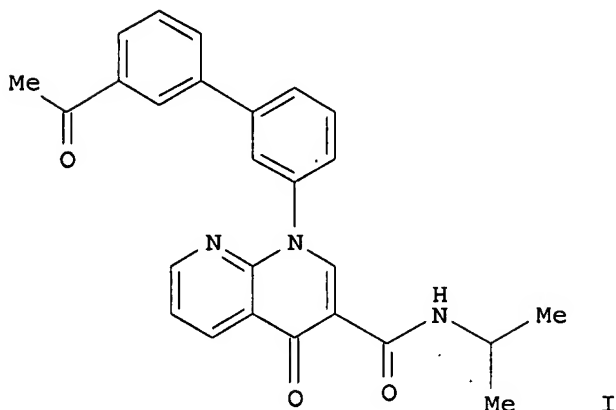
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004048377	A2	20040610	WO 2003-US36806	20031118
	WO 2004048377	A3	20040902		
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	RW:				
	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2506656	A1	20040610	CA 2003-2506656	20031118
	AU 2003291050	A1	20040618	AU 2003-291050	20031118
	EP 1565466	A2	20050824	EP 2003-783636	20031118
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003016464	A	20051011	BR 2003-16464	20031118
	CN 1738818	A	20060222	CN 2003-80108946	20031118
	JP 2006513271	T	20060420	JP 2005-510366	20031118
	US 2006019981	A1	20060126	US 2005-530465	20050405
	NO 2005003047	A	20050810	NO 2005-3047	20050621
PRAI	US 2002-428315P	P	20021122		
	US 2003-472655P	P	20030522		
	WO 2003-US36806	W	20031118		
OS	MARPAT 141:38597				
IT	500355-52-2P				

RL: IMF (Industrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of aryl substituted 1,8-naphthyridin-4(1H)-ones as inhibitors of phosphodiesterase-4)

RN 500355-52-2 CAPLUS

CN 1,8-Naphthyridine-3-carboxamide, N-cyclopropyl-1,4-dihydro-1-[3-[2-(1-oxido-3-pyridinyl)ethynyl]phenyl]-4-oxo- (CA INDEX NAME)

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
GI

AB. Substituted naphthyridines are prepared as PDE-4 inhibitors. For instance, Et 3-(3-bromoanilino)-2-(2-chloronicotinoyl)acrylate (preparation given) is treated with NaH in THF to give Et 1-(3-bromophenyl)-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxylate. This intermediate is saponified, coupled to i-PrNH<sub>2</sub> (THF, Et<sub>3</sub>N, i-BuOCOC1) and coupled to 3-acetylphenylboronic acid (PhMe, EtOH, Na<sub>2</sub>CO<sub>3</sub>, trans-dibromobis(triphenylphosphine)palladium, reflux, 1 h) to give I. Example compds. have IC<sub>50</sub> values of 0.1 to 90.0 nM for PDE4; these compds. are useful for enhancing memory, learning, retention, recall, awareness and judgement.

AN 2004:467741 CAPLUS

DN 141:38595

TI Preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition

IN Dube, Daniel; Gallant, Michel; Lacombe, Patrick; Girard, Yves; MacDonald,

Dwight; Friesen, Richard; Ducharme, Yves; Cote, Bernard; Blouin, Marc;  
Martins, Evelyn; Guay, Daniel; Girard, Mario; Frenette, Richard;  
Laliberte, Sebastien; Robichaud, Annette; Mastracchio, Anthony; Perrier,  
Helene

PA Merck Frosst Canada & Co., Can.; Hamel, Pierre

SO PCT Int. Appl., 138 pp.

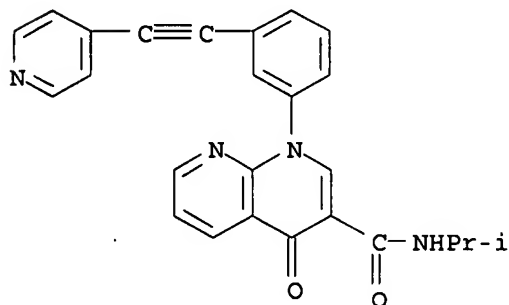
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004047836	A1	20040610	WO 2003-CA1799	20031119
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	AU 2003286024	A1	20040618	AU 2003-286024	20031119
	EP 1592419	A1	20051109	EP 2003-776698	20031119
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006040981	A1	20060223	US 2005-536250	20050520
PRAI	US 2002-428541P	P	20021122		
	WO 2003-CA1799	W	20031119		
IT	500355-39-5P, N-Isopropyl-1-[3-[(pyridin-4-yl)ethynyl]phenyl]-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide				
	RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)				
	(preparation of substituted naphthyridine phosphodiesterase-4 inhibitors as enhancers of cognition)				
RN	500355-39-5 CAPLUS				
CN	1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)				



RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

AB The title 1-phenyl-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide derivs. are prepared as phosphodiesterase 4 (PDE4) inhibitors. For example, N-isopropyl-1-[3-(phenylethynyl)phenyl]-1,4-dihydro-[1,8]naphthyridin-4-one-3-carboxamide was prepared in a multi-step synthesis comprising a ring-closure reaction. The title compds., in conjunction with psychotherapy, provide enhanced therapeutic results in the treatment of psychiatric disorders including specific phobias, panic disorders, anxiety disorders including posttraumatic stress disorders, and obsessive-compulsive disorder (no data).

AN 2004:452951 CAPLUS

DN 141:23432

TI Preparation of 1-phenyl-1,4-dihydro[1,8]naphthyridin-4-one-3-carboxamide derivatives as PDE4 inhibitors for treatment of psychiatric disorders

IN Scolnick, Edward M.

PA Merck & Co., Inc., USA

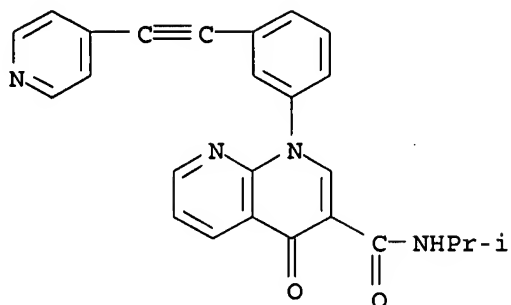
SO PCT Int. Appl., 40 pp.  
CODEN: PIXXD2

DT Patent

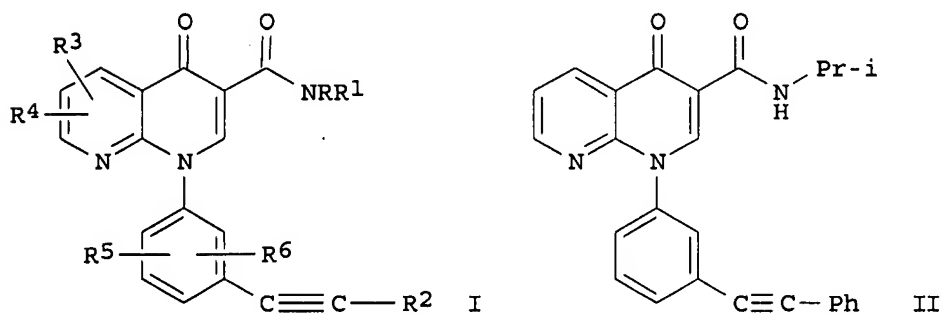
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045508	A2	20040603	WO 2003-US35718	20031110
	WO 2004045508	A3	20050324		
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	RW:				
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	AU 2003291418	A1	20040615	AU 2003-291418	20031110
	EP 1562588	A2	20050817	EP 2003-768815	20031110
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2006069115	A1	20060330	US 2005-530841	20050408
PRAI	US 2002-426529P	P	20021115		
	WO 2003-US35718	W	20031110		
IT	500355-39-5P				
	RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (drug candidate; preparation of dihydro[1,8]naphthyridinone derivs. as PDE4 inhibitors for treatment of psychiatric disorders)				
RN	500355-39-5 CAPLUS				
CN	1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-(4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)				



L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN  
GI



AB Alkyne-aryl 1,8-naphthyridin-4(1H)ones of formula I [R = H, alkyl, cycloalkyl; R1 = H, alkyl, cycloalkyl, alkoxy, acyl, Ph, heteroaryl, etc.; R2 = H, (substituted) Ph, pyridyl, pyrimidinyl, indolyl, quinolinyl, thienyl, etc. and oxides thereof; R3-R6 = H, halo, alkyl, alkoxy, nitro, CN, etc.] are prepared as phosphodiesterase 4 inhibitors useful in the treatment of asthma and inflammation. Thus, II was prepared from Et 2-chloronicotinoyl acetate, 3-bromoaniline, isopropylamine and phenylacetylene. The prepared compds. inhibited the hydrolysis of cAMP with IC50 of 0.1 nM to 90.0 nM.

AN 2003:173603 CAPLUS

DN 138:205042

TI Preparation of alkyne-aryl 1,8-naphthyridin-4(1H)ones as phosphodiesterase-4 inhibitors

IN Guay, Daniel; Girard, Mario; Hamel, Pierre; Laliberte, Sebastien; Friesen, Richard

PA Merck Frosst Canada & Co., Can.

SO PCT Int. Appl., 80 pp.

CODEN: PIXXD2

DT Patent

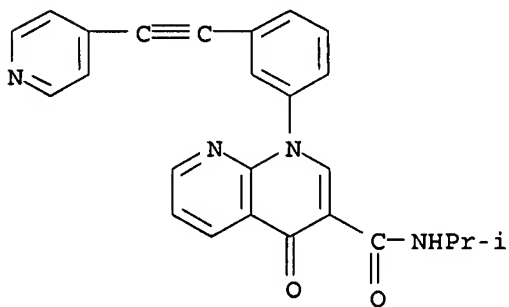
LA English

FAN.CNT 1

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PI	WO 2003018579	A1	20030306	WO 2002-CA1324	20020827
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				



CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,  
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,  
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,  
 UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,  
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,  
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,  
 NE, SN, TD, TG  
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 AU 2002322940 A1 20030310 AU 2002-322940 20020827  
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 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
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 NO 2004001293 A 20040527 NO 2004-1293 20040326  
 PRAI US 2001-316093P P 20010829  
 WO 2002-CA1324 W 20020827  
 OS MARPAT 138:205042  
 IT 500355-39-5P  
 RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation of alkyne-aryl naphthyridinones as phosphodiesterase 4  
 inhibitors)  
 RN 500355-39-5 CAPLUS  
 CN 1,8-Naphthyridine-3-carboxamide, 1,4-dihydro-N-(1-methylethyl)-4-oxo-1-[3-  
 (4-pyridinylethynyl)phenyl]- (9CI) (CA INDEX NAME)



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT